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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/606,190	06/25/2003	Kevin Thorne	SBI-129	2194
45488	7590	06/10/2005	EXAMINER	
WILLIAMS, MORGAN & AMERSON, P.C./ZIMMER 10333 RICHMOND, SUITE 1100 HOUSTON, TX 77042			AFREMOVA, VERA	
			ART UNIT	PAPER NUMBER
			1651	

DATE MAILED: 06/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/606,190

Applicant(s)

THORNE, KEVIN

Examiner

Vera Afremova

Art Unit

1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 5/09/2005.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-24 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-24 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>5/03/04; 5/26/04</u> . | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

Claims 1-24 are pending and under examination.

#### ***Claim Rejections - 35 USC § 112***

Claims 11, 12 and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 lacks a proper antecedent basis for the term “mineralized supernatant solution” in the method of claim 9 because claim 9 recites a “mineral-containing acid supernatant”. The differences between these two solutions and/or supernatants are uncertain as claimed.

Claim 24 lacks proper antecedent basis for the term “the protein supernatant solution” in step(s) preceding the step of extracting.

#### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 9-19 and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by US 4,294,753 (Urist).

Claims are directed to a method of obtaining osteogenic proteins from mammalian bone tissue wherein the method comprises contacting bone tissue with an acidic medium, separating a demineralized bone tissue and a solution of mineralized supernatant and further recovering

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and/or purifying osteogenic proteins from the solution of mineralized supernatant by extracting proteins with extracting agents. Some claims are/are further drawn to the recovering or purifying osteogenic proteins by filtering the extracted proteins with high and low MW cut of membranes. Some claims are further drawn to the use of guanine hydrochloride and/or urea as protein extracting agents. Some claims are further drawn to recovering or purifying the osteogenic proteins by diafiltration, by precipitating minerals with calcium oxalate. Some claims are further drawn to the acidic medium such as hydrochloric acid. Some claims are further drawn to lyophilization of the extracted/recovered/purified proteins.

US 4,294,753 (Urist) teaches a method of obtaining osteogenic proteins from mammalian bone tissue wherein the method comprises identical processing steps of demineralization of bone tissue in acidic medium or hydrochloric acid (col. 3, lines 1-5), steps of extracting proteins with urea or guanidine (col. 3, lines 19-20), steps of high and low MW filtration (col. 4, lines 1-10); further steps of purifying the extracted proteins by diafiltration with urea solution, by precipitating minerals with calcium salts including calcium oxalate (col. 3, line 50), by redissolving and reprecipitating the extracted proteins (col. 3, lines 34-45) including redissolving with acid (col. 3, lines 54) and step of lyophilization (col. 4, line 37). The cited patent teaches both processing steps 1) recovering osteogenic proteins from a bone matrix that is demineralized with acidic medium or hydrochloric acid (see figure) and 2) recovering osteogenic proteins from a supernatant hydrochloric acid solution or from a "solution of mineralized supernatant" that is separated from demineralized bone matrix (col. 3, lines 7-10). Thus, the cited patent anticipates the claimed invention.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 4,294,753 (Urist) and US 5,371,191 (Poser et al.) and US 4,619,989 (Urist).

Claims 1-5, 9-19 and 24 as above. Some claims are further drawn to additional purification steps including diafiltration to remove guanidine and urea and/or to additional purification steps including redissolving and reprecipitating proteins in solvents including diluted acid, HCl and acetone.

US 4,294,753 (Urist) is relied upon as explained above and it teaches a method of obtaining osteogenic proteins from mammalian bone tissue wherein urea is a preferred protein-extracting agent (see figure). It also teaches that both protein-extracting agents including guanidine and urea can be used in the method of obtaining osteogenic proteins from mammalian bone tissue (col. 3, line 20). Thus, US 4,294,753 (Urist) is lacking a particular disclosure when both protein-extracting agents guanidine and urea are both used in the same or one protocol of recovering osteogenic proteins.

However, US 5,371,191 (Poser et al.) teaches the use of guanidine as protein-extracting agent in the similar method of obtaining osteogenic proteins from mammalian bone tissue wherein the method comprises high and low MW cut off filtration steps of proteins extracted

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with guanidine. The cited US 5,371,191 (Poser et al.) also teaches further purification steps such as diafiltration to substitute urea for guanidine (col. 3, line 45).

Although the method of US' 191 encompasses protein extraction with guanidine from bone matrix that is demineralized with acidic medium but not from mineralized acidic supernatant, the cited US' 753 teaches protein extraction from mineralized acidic supernatant.

Both US 4,294,753 (Urist) and US 5,371,191 (Poser et al.) teach lyophilization of recovered proteins and additional purification steps including redissolving and reprecipitating in various solvents including water and dilute acids (US' 753, see figure) and including hydrochloric acid (US' 191, see col. 10, lines 59-59-64).

Although the cited US 4,294,753 (Urist) and US 5,371,191 (Poser et al.) are silent about the use of acetone, the other Urist's patent (US 4,619,989) discloses that osteogenic proteins BMPs are insoluble in organic solvents including acetone. Thus, acetone washing of the final semi-pure preparations of BMPs would be obvious to practitioners with ordinary skill in the art and they would be motivated to do so for the expected benefits in removing from BMPs those impurities that are soluble in acetone.

Therefore, the claimed inventions taken as a whole would have been obvious to one having ordinary skill in the art at the time the claimed invention was made because all processing steps in the method of obtaining osteogenic proteins from mammalian bone tissue as encompassed by the presently claimed invention are taught and suggested by the prior art as adequately demonstrated by the cited references. Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

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The claimed subject matter fails to patentably distinguish over the state art as represented by the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926.

The fax phone number for the TC 1600 where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology center 1600, telephone number is (571) 272-1600.

Vera Afremova

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June 7, 2005

A handwritten signature in black ink, appearing to read 'V. Afremova', with a long horizontal flourish extending to the right.

VERA AFREMOVA

PRIMARY EXAMINER